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Annual Review of Medicine

A Rational Approach to the Treatment of Acute Pulmonary Embolism

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Annu. Rev. Med. 2025. 76:327–37

First published as a Review in Advance on January 2, 2025

The *Annual Review of Medicine* is online at med.annualreviews.org

https://doi.org/10.1146/annurev-med-050423-085457

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Keywords

pulmonary embolism, anticoagulation, embolectomy, thrombolytics

Abstract

Over the past decade, new modalities have emerged to treat acute pulmonary embolism (PE). However, PE remains a leading cause of morbidity and mortality worldwide. In the absence of robust clinical trial data and definitive guidelines and recommendations for a variety of clinical situations, individual patient treatment decisions have become paradoxically more challenging as innovation in the space has grown. In this review, we discuss a practical and current approach to patients diagnosed with PE, focusing on their risk stratification and treatment selection.

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INTRODUCTION

Pulmonary embolism (PE) ranks as the third leading cause of cardiovascular death in the United States, following myocardial infarction and stroke (1). It accounts for approximately 40,000 deaths annually, with acute mortality rates ranging from 3.7% to 20.6% in hospitalized patients without and with hemodynamic instability, respectively (2). Timely diagnosis and initiation of treatment are crucial for improving outcomes. Over the past couple of decades, there has been a notable increase in PE diagnoses, likely attributable to enhanced vigilance among physicians and the more widespread and prompt utilization of computed tomography (CT) imaging (3). Once PE has been diagnosed, the treatment depends on careful and dynamic risk stratification based on clinical assessment and predictive models that consider both in-hospital and 30-day morbidity and mortality. While anticoagulation remains fundamental for the treatment of acute PE and prevention of new episodes, the therapeutic landscape has recently expanded to include various invasive interventions such as surgical or percutaneous embolectomy and catheter-directed thrombolysis (CDL). With more options at our disposal, the approach to the treatment of PE is becoming more nuanced, and the type and timing of treatments are increasingly tailored to individual patients and their clinical evolution. This review aims to explore the available treatment options and emphasize a rational approach to PE management based on careful risk stratification.

PATIENTS' RISK STRATIFICATION AND CLASSIFICATION OF PULMONARY EMBOLISM

The contemporary classifications of PE have been outlined by the American Heart Association/American College of Cardiology (AHA/ACC) and the European Society of Cardiology (ESC) in their respective consensus statements. For this review's purposes, the ESC criteria are utilized. The ESC schema categorizes PE into low, intermediate, and high risk of 30-day mortality (4, 5). This classification hinges not only on the patient's blood pressure but also on the impact of PE on the right ventricle (RV).

Acute RV failure resulting from a substantial increase in PE-induced afterload is recognized as the primary cause of death in PE. Early indicators of the detrimental cascade initiated by an acute rise in RV afterload include RV dilation and increased RV wall tension. Left untreated, these manifestations can progress to neurohormonal activation, RV ischemia, hemodynamic compromise, and ultimately cardiovascular collapse. Therefore, early recognition of RV dilation, either on the index CT PE protocol [assessed by the RV/left ventricle (LV) ratio] or via transthoracic echocardiogram, is critical for risk stratification. The RV/LV ratio has also emerged as a surrogate marker to evaluate treatment efficacy in clinical trials. Patients presenting with hemodynamic instability almost invariably have significant RV compromise and are classified as high-risk PE. Clinical markers of hemodynamic instability include a systolic blood pressure <90 mmHg, a drop in systolic blood pressure of >40 mmHg for at least 15 min, the necessity for vasopressor support or mechanical circulatory support, persistent profound bradycardia <40 bpm, and cardiac arrest. Patients with hemodynamic collapse necessitating emergent escalation of care or high-dose vasopressors and those sustaining cardiac arrest as the index event or soon after hospitalization represent a subset of high-risk PE patients that is categorized as catastrophic PE (2).

Patients who do not meet the criteria for hemodynamic instability must undergo further risk stratification based on right ventricular function and markers of myocardial injury or pressure overload [such as troponin and brain natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP)]. If both RV dilation, ascertained by echocardiogram or CT, and biomarker abnormalities are present, the patient is classified as intermediate-high risk. If only one of the two criteria is met, the patient is deemed intermediate-low risk. Lastly, if neither RV dilation

nor biomarker abnormalities are present, the patient is categorized as low risk of 30-day mortality. In addition to hemodynamic parameters, imaging, and laboratory findings, baseline characteristics and comorbidities can contribute to worse outcomes and should be considered when assessing a patient's overall mortality risk.

The Pulmonary Embolism Severity Index (PESI) and its simplified version, sPESI, are the most extensively validated scores that integrate PE severity and preexisting comorbidities. The PESI risk score incorporates age, gender, pertinent medical history characteristics (such as heart failure, history of cancer, and chronic lung disease), acute hemodynamic parameters (including heart rate, systolic blood pressure, respiratory rate, temperature, and oxygen saturation), and the patient's mental status. It reliably identifies patients at low risk for 30-day mortality and therefore was integrated in the 2019 ESC guidelines on the diagnosis and management of PE (4). In patients with neither RV dilation nor biomarker elevation, who would otherwise be deemed to be at low risk, a PESI score of 3 or higher conveys a worse prognosis and reclassifies them as intermediate-low risk of 30-day mortality. Lastly, based on clinical evolution, patients' risk profiles might dynamically evolve over time, necessitating ongoing reassessment and the potential adjustment of therapeutic strategies (**Figure 1**).

SPECIAL CONSIDERATIONS REGARDING RISK ASSESSMENT

Categorizing patients into these risk strata carries profound prognostic implications that guide both the nature and timing of intervention, as well as the level of care required. However, it is important to acknowledge the limitations of algorithmic risk stratification and emphasize the necessity of individualized assessment for each patient. For instance, PE is often an incidental finding in critically ill patients where its repercussions on the overall clinical scenario might be limited in the absence of a corresponding acute clinical change (6). Although preexisting cardiac or pulmonary conditions can exacerbate the hemodynamic effects of PE, they can also introduce complexities in interpreting imaging or laboratory data. For example, in patients with chronic obstructive pulmonary disease or chronic pulmonary hypertension with RV dilation, identifying significant changes in RV size and function can be challenging, potentially leading to an over- or underestimation of the risk posed by the PE. Similarly, elevated levels of troponin and BNP/NT-proBNP may be linked to preexisting conditions such as cardiomyopathy, volume overload, or end-stage renal disease, potentially obscuring our assessment of PE-related risk (7). In these cases, it is important to consider the location of the emboli (central or peripheral) and the estimated clot burden to verify that the RV dysfunction or biomarker abnormalities can be reasonably explained by the anatomical characteristics of the acute PE. Conversely, significant discrepancies should raise the suspicion that concomitant chronic comorbidities might be responsible for the findings.

TREATMENT OF ACUTE PULMONARY EMBOLISM

Respiratory and Hemodynamic Support

Patients with PE can present with varying degrees of hypoxemia due to a ventilation/perfusion mismatch. Oxygen therapy is recommended for patients with oxygen saturation levels below 90%. Noninvasive ventilation methods, including nasal cannula, Venturi mask, or high-flow oxygen, are generally well tolerated; however, they may not completely correct hypoxemia until the ventilation/perfusion mismatch is resolved. In cases of intermediate- or high-risk PE, escalation to mechanical ventilation should be approached with caution, as it carries a significant risk of hemodynamic decompensation secondary to severe hypotension during induction anesthesia. Positive-pressure ventilation can also decrease RV preload, potentially exacerbating the

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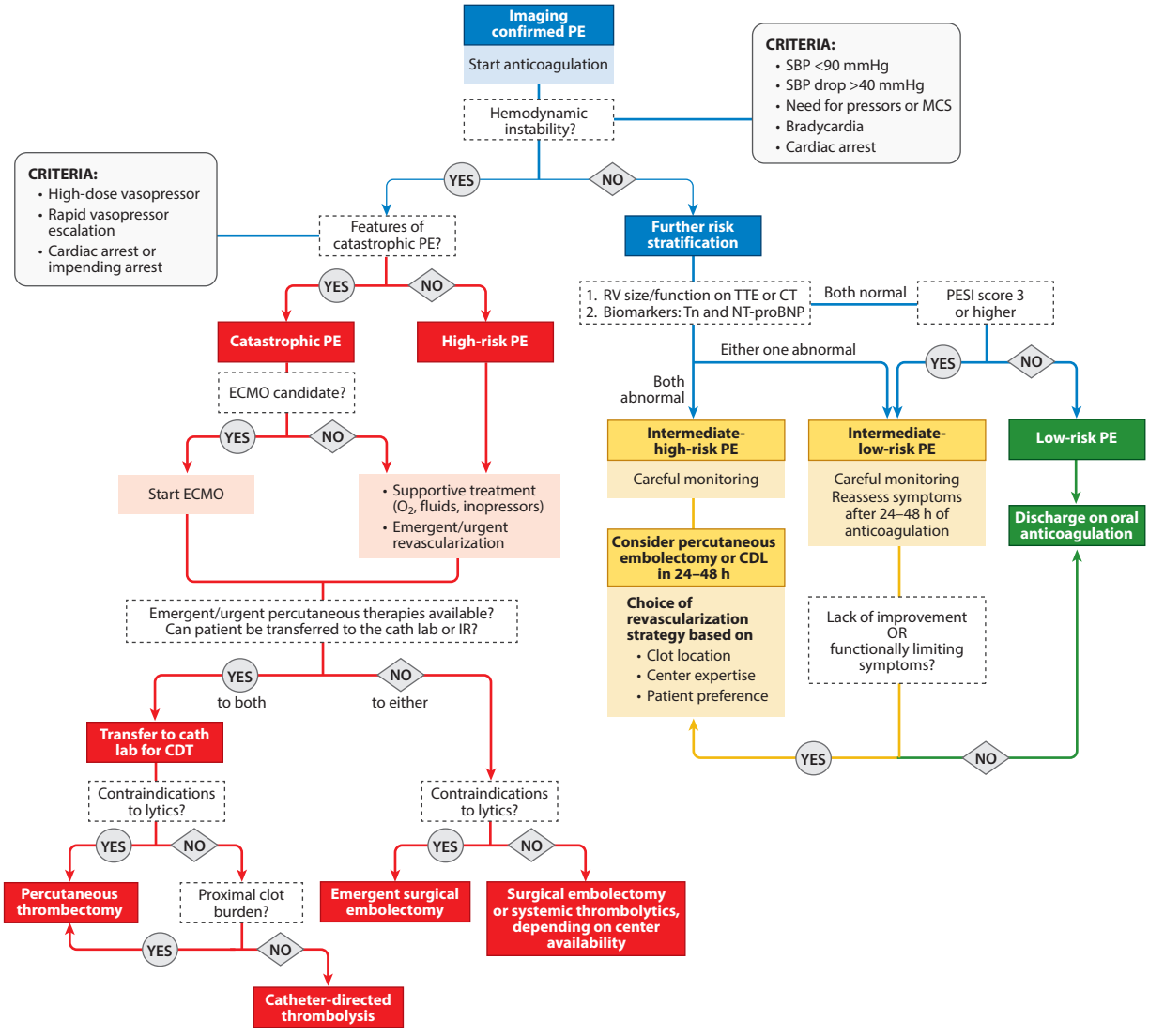

Figure 1

Proposed management algorithm. Abbreviations: CDL, catheter-directed thrombolysis; CDT, catheter-directed therapy (including CDL and percutaneous embolectomy); CT, computed tomography; ECMO, extracorporeal membrane oxygenation; IR, interventional radiology; MCS, mechanical circulatory support; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PE, pulmonary embolism; PESI, Pulmonary Embolism Severity Index; RV, right ventricle; Tn, troponin; TTE, transthoracic echocardiogram; SBP, systolic blood pressure.

reduction in cardiac output. If mechanical ventilation becomes absolutely necessary, providers should be ready to support the patient with venoarterial extracorporeal membrane oxygenation (VA-ECMO) in case of acute decompensation and have concomitant plans for urgent reperfusion treatments if available (4). In cases of shock, the use of inotropes may be necessary. Pure vasopressors should be avoided as they can exacerbate pulmonary vascular resistance. Conversely, norepinephrine improves systemic vascular resistance without increasing pulmonary vascular resistance and has become the inopressor of choice in PE (8). Nevertheless, both pharmacological

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and mechanical support are temporizing measures that serve to stabilize the patient while more definitive treatment for PE is considered and initiated.

Anticoagulation and Advanced Treatment Strategies

At present, anticoagulation as the initial up-front strategy is recommended regardless of the clinical risk stratification of the PE. All other treatment options, including systemic thrombolytics, CDL, surgical embolectomy, and transcatheter embolectomy, are considered advanced therapies for PE.

Systemic anticoagulation. Anticoagulation is the cornerstone treatment of PE aimed at preventing local thrombus extension and new thrombi from forming in the lower extremities. It should be initiated as soon as possible in patients with diagnosed PE or in those with a high clinical suspicion and an acceptable risk of bleeding. Enoxaparin and fondaparinux are preferred over unfractionated therapy, when possible, to ensure a rapid and steady anticoagulating effect. Upon discharge or once the need for invasive interventions is excluded, oral anticoagulation with direct oral anticoagulants (DOACs) or a vitamin K antagonist should be started.

When compared to vitamin K antagonists, DOACs have demonstrated noninferiority in preventing recurrent PE while also carrying a lower risk of bleeding (9, 10). Due to these advantages and their ease of use, DOACs have largely replaced vitamin K antagonists for this indication. However, in cases where vitamin K antagonists are still employed, bridging with enoxaparin is recommended until a therapeutic international normalized ratio above 2 is achieved.

Systemic thrombolysis. Systemic thrombolysis uses recombinant tissue-type plasminogen activators (tPAs) to convert plasminogen to plasmin and rapidly dissolve the embolic burden. However, this approach is accompanied by a potentially catastrophic risk of bleeding. A meta-analysis of 16 trials comprising 2,115 patients with high- and intermediate-risk PE (340 and 1,775 subjects, respectively) treated with routine administration of systemic thrombolytics demonstrated a significant reduction in mortality rate compared to anticoagulation alone, with a number needed to treat of 54. Nonetheless, systemic thrombolysis carried a threefold higher risk of major bleeding, with a number needed to harm (NNH) of only 18. Most concerningly, patients treated with systemic thrombolysis had a 1.46% rate of intracranial hemorrhage, which represented a risk 4.6 times higher than anticoagulation only [odds ratio (OR), 4.63; 95% confidence interval (CI), 1.78–12.04; NNH, 78). Notably, these results were primarily driven by bleeding events in patients over 65 years of age, whereas for those under 65, the bleeding risk seemed comparable to that of anticoagulation alone (11). These results have led to reserving systemic thrombolysis for hemodynamically significant PE, in which the risk of life-threatening bleeding can be offset by the mortality benefit of immediate treatment in settings where invasive therapies are not immediately accessible. In an effort to reduce the risk of catastrophic bleeding, various doses and infusion durations of systemic thrombolysis have been tested. A large meta-analysis of randomized clinical trials comprising 440 patients treated with either reduced-dose (0.6 mg/kg, maximum 50 mg or 50 mg infusion 2 h) or standard-dose (100 mg infusion 2 h) tPA showed no difference in recurrent PE and mortality between the two regimes. However, reduced-dose thrombolytics were associated with a lower risk of bleeding compared with the standard dose (OR, 0.33; 95% CI, 0.12–0.91; $p = 0.94$) (12).

In summary, current clinical guidelines recommend the full dose of tPA in patients presenting with high-risk PE and without contraindications to tPA. However, routine use of systemic thrombolysis should be avoided in intermediate-risk PE. Reduced doses could be considered in specific groups such as elderly patients or pregnant women. Prior to initiating thrombolytic treatment with any protocol, meticulous patient selection and assessment of the risk–benefit ratio are

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imperative. When available, multidisciplinary PE response teams can provide valuable assistance in determining the appropriate use and timing of thrombolytics.

Catheter-directed thrombolysis. Catheter-directed thrombolysis (CDL), in which thrombolytic therapy is administered over 12 to 24 h directly into target pulmonary arteries via catheters, has emerged as a promising alternative to systemic thrombolytics. CDL includes standard local thrombolysis through small multihole catheters and ultrasound-assisted thrombolysis in which ultrasound waves emitted by specialized catheters facilitate the penetration of the thrombolytic agent into the thrombus. In a small randomized head-to-head comparison between the two CDL strategies, no significant difference in efficacy was found related to thrombotic burden at 48 h assessed by the modified Miller index. There was a greater improvement in the RV/LV ratio at 48 h in the standard CDL group, although that should be interpreted in the context of a small sample size (80 patients in total) (13). Nonetheless, the majority of evidence regarding the safety and efficacy of CDL comes from trials on ultrasound-assisted thrombolysis. For instance, the Seattle II single-arm study enrolled 150 patients with intermediate-risk PE treated with ultrasound-facilitated CDL. The study demonstrated CDL to be safe with no intracranial hemorrhage and only a 0.7% incidence of severe Global Use of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) bleeding. The treatment was also effective in clot debulking, as assessed by the modified Miller index, and led to a rapid reduction in the RV/LV ratio (14). When tested in a randomized clinical trial against anticoagulation alone, ultrasound-facilitated CDL was superior in reversing RV dilatation at 24 h, without an increase in bleeding complications. Registry data from larger patient cohorts appear to corroborate these findings, showing improvements in mean pulmonary artery pressure and right ventricular function (15). Despite these encouraging results, we still lack randomized clinical trial data on hard clinical outcomes such as hemodynamic decompensation, bleeding, and mortality, compared with anticoagulation or other advanced treatments. However, important ongoing randomized clinical trials aim to address whether up-front CDL is more beneficial than anticoagulation alone or other modalities in intermediate-risk PE. A list of ongoing randomized clinical trials on PE treatments is provided in **Table 1**.

Surgical embolectomy. Removal of the thrombus from the pulmonary artery represents a mechanical solution to a mechanical problem. Surgical thrombectomy, in its current technique, has a postoperative in-hospital mortality rate ranging from 2.3% to 13.2%, with worse outcomes in patients requiring cardiopulmonary resuscitation. Given the paucity of randomized data, these mortality rates might reflect the acuity and heterogeneity of patients' presentation more than the efficacy of the procedure. Retrospective studies on the use of surgical embolectomy in both hemodynamically stable and unstable patients showed improvement in central venous pressures, normalization of RV dilation, and improved survival rates. In experienced centers, outcomes with surgical embolectomy for high-risk patients appear excellent, but there is a paucity of such centers in the United States. Thus, it is typically reserved for hemodynamically significant PE in patients with contraindications to fibrinolytics or in whom other interventions have failed (16, 17).

Transcatheter embolectomy options. By comparison, transcatheter embolectomy is a lower-risk procedure that is becoming more widespread. Several devices have been developed for transcatheter embolectomy in recent years. They are all moderate- to large-bore devices (12 to 25 Fr) that perform suction embolectomy with or without adjunctive mechanical mobilization or fragmentation. In centers with adequate expertise and where this procedure is readily available, percutaneous embolectomy offers a valuable option to avoid the risk of systemic thrombolysis for patients with hemodynamically significant PE.

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Table 1 Ongoing randomized clinical trials on pulmonary embolism treatment

Trial name	Trial type	Number of patients	PE risk category	Arm 1	Arm 2	Primary outcomes
PEERLESS I NCT05111613	Phase III multicenter	550	Intermediate-high	Perc. embolectomy with FlowTriever plus AC	CDL	Composite clinical endpoint constructed as a win ratio, including ■ mortality ■ intracranial hemorrhage ■ major bleeding per the ISTH definition ■ hemodynamic or respiratory worsening and/or escalation to a bailout therapy ■ ICU admission and ICU length of stay during the index hospitalization
PEERLESS II NCT06055920	Phase III multicenter	1,200	Intermediate	Perc. embolectomy with FlowTriever plus AC	AC alone	Composite clinical endpoint constructed as a win ratio, including ■ hemodynamic or respiratory worsening ■ all-cause rehospitalization ■ bailout therapy ■ dyspnea, by the mMRC scale
PE-TRACT NCT05591118	Phase III multicenter	500	Intermediate	CDT plus AC	AC alone	PVO2 uptake at 3 months (via CPET); NYHA class at 12 months; Composite of major bleeding, major cardiovascular or pulmonary injury, and major procedure-related serious adverse events
HI-PEITHO NCT04790370	Phase IV multicenter	544	Intermediate-high	CDL with USAT plus AC	AC alone	Composite of mortality, cardiorespiratory decompensation or collapse, or nonfatal symptomatic and objectively confirmed PE recurrence within 7 days
STORM-PE NCT05684796	Multicenter	100	Intermediate-high	Perc. embolectomy (with Penumbra) plus AC	AC alone	RV/LV ratio change in 24 h
PRAGUE-26 NCT05493163	Phase IV multicenter	558	Intermediate-high	Standard CDL plus AC	AC alone	Composite of all-cause mortality, PE recurrence, or cardiorespiratory decompensation within 7 days of randomization
PEITHO3 NCT04430569	Phase III	650	Intermediate-high	Low-dose alteplase plus AC	AC alone	Composite of death from any cause, hemodynamic decompensation, or objectively confirmed recurrent PE within 30 days
CATCH-PE NCT05456789	Phase II single center	20	Intermediate-high	Perc. embolectomy plus local fibrinolysis	AC alone	RV/LV ratio change in 24 h; Quotient of systolic systemic blood pressure over heart rate and respiratory rate
BETULA NCT03854266	Phase II	60	Intermediate-high	CDL (4 mg alteplase per catheter over 2 h) plus AC	AC alone	RV/LV ratio change in 24 h
STRATIFY NCT04088292	Phase III multicenter	210	Intermediate-high	USAT plus AC versus low-dose systemic lysis	AC alone	Reduction in Miller score at 48 h and 96 h
NAIL-IT NCT05408546	Phase II	32	Intermediate	TS23, a novel α2-antiplasmin inactivator	Placebo	RV/LV at 48 h; Major or clinically significant bleeding within 7 days
SAFE-SSPE NCT04263038	Phase IV multicenter	276	Low- subsegmental PE	Rivaroxaban	Placebo	Recurrent venous thromboembolism

Abbreviations: AC, anticoagulation; CDL, catheter-directed thrombolysis; CDT, catheter-directed therapy (including CDL and percutaneous embolectomy); CPET, cardiopulmonary exercise testing; ICU, intensive care unit; ISTH, International Society of Thrombosis and Haemostasis; LV, left ventricle; mMRC, modified Medical Research Council; NYHA, New York Heart Association; PE, pulmonary embolism; perc., percutaneous; PVO2, peak oxygen consumption; RV, right ventricle; USAT, ultrasound-assisted thrombolysis.

Treatment of Pulmonary Embolism According to Risk Group

Management for PE differs based upon the severity of the patient's clinical scenario.

Catastrophic and high-risk pulmonary embolism. Although high-risk PEs constitute only 5% of total cases, they are associated with the highest mortality rates, averaging between 20% and 32% and reaching 65% in cases of catastrophic PE with cardiac arrest (2). Treatment choice depends on both patient-specific and center-specific factors. While the ESC practice guidelines suggest systemic thrombolysis as a first-line therapy, based upon availability and access, our own and other leading US institutions consider other advanced therapy options prior to systemic thrombolysis. In patients who present with or escalate to catastrophic PE mechanical circulatory support (with VA-ECMO), candidacy is first considered as a means to off-load the RV, fully supporting the patient from both a circulatory and oxygenation standpoint. Utilization of VA-ECMO in selected cases allows for clinical stabilization prior to any other decisions needing to be made. Thereafter, urgent or emergent catheter-directed or surgical therapies are considered in both patients with high-risk PE and those with catastrophic PE stabilized on VA-ECMO. Decisions on revascularization strategy include the assessment for contraindication to thrombolytic therapy, anatomical targets for catheter-directed embolectomy, and perceived complications and comorbidities that raise the risk for surgical embolectomy. In centers with readily available transcatheter therapies (embolectomy and CDL), these are becoming the treatment of choice in addition to early initiation of anticoagulation. Surgical embolectomy is most commonly reserved for patients with failed systemic thrombolytics or those who fail to demonstrate clinical improvement during or after employment of transcatheter approaches. With the increasing number of centers offering percutaneous intervention for PE and the ongoing trials on various catheter-directed therapies, we anticipate that the therapeutic algorithm proposed in the current guidelines will be adjusted over the next several years to reflect the new evidence and clinical practice (16) (**Figure 1**).

Intermediate-risk pulmonary embolism. Intermediate-risk PE accounts for approximately 30% of PE cases, with a mortality ranging from 2% in patients with only biomarker abnormalities to 10% in those with both RV dilation and altered biomarkers (18). In patients presenting without systemic hypotension or hemodynamic compromise, standard anticoagulation is generally considered first-line treatment. However, 5–10% of patients classified as having intermediate-high risk PE further progress to hemodynamic instability during hospitalization. Given the pathophysiology of PE, it is recognized that hypotension can be a late manifestation of severe disease. Thus, focusing solely on blood pressure is not sufficient to determine clinical stability and identify patients at risk of progressing between risk strata. Several additional criteria are considered in the evaluation of this group of patients, including elevated venous lactate levels indicating tissue malperfusion, tachycardia, significant hypoxia, limitation in very mild exertion (e.g., rising from bed and using the bathroom), hypoxia, and mobile intracardiac clot in transit. Careful monitoring of all clinical parameters and their dynamic changes is critical in these patients. Our limited ability to predict clinical progression, coupled with the availability of catheter-based interventions carrying acceptable risks, supports the consideration of invasive treatment in select patients on the higher end of the intermediate-risk spectrum following prompt initiation of anticoagulation (**Figure 1**).

This is an active area of investigation, however, in regard to the modality and timing of intervention for intermediate-high-risk PE patients (19, 20). HI-PEITHO (NCT047903700) and PEERLESS II (NCT06055920) are ongoing large randomized clinical trials enrolling patients with intermediate-high-risk PE (21, 22). PEERLESS II will investigate transcatheter embolectomy with FlowTriever versus anticoagulation alone while HI-PEITHO will compare

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ultrasound-assisted thrombolysis versus anticoagulation alone. Both focus on short- to intermediate-term outcomes with clinically relevant primary outcomes focused on the in-hospital period and ongoing follow-up until 90 days after randomization. Similarly, PE-TRACT is actively enrolling intermediate-risk patients and randomizing them to catheter-directed therapies (CDL or percutaneous thrombectomy) or anticoagulation alone (**Table 1**). The focus of this study is on intermediate- to long-term clinical outcomes (3–12 months after randomization).

In those on the lower end of the intermediate-risk spectrum, the necessity and future for invasive interventions are uncertain. It could be reasonable to consider catheter-based interventions in patients with a high PESI score or functionally limiting symptoms that do not improve after 24 to 48 h of systemic anticoagulation, but randomized data will need to emerge to support such strategies. Further, in intermediate-risk patients who qualify for both CDL and catheter-directed embolectomy, the relative risk–benefit profile across a range of outcomes is uncertain. The PEERLESS trial (NCT05111613), which recently completed the enrollment of 550 subjects, aims to address this issue (23). Lastly, we find ourselves amid a renaissance of development and innovation in PE therapies, with a host of novel devices under study aiming to optimize catheter-directed embolectomy and CDL approaches. Over the next several years, considerable technical innovation is expected that will ideally improve the safety, efficacy, and efficiency of endovascular treatment of the disease process.

Low-risk pulmonary embolism. Patients with low-risk PE make up approximately 60% of identified cases. Frequently, these patients are minimally symptomatic and may not require hospital admission, particularly if their PESI score is <3. Outpatient management is feasible in such cases, with oral anticoagulation commenced promptly. Conversely, those with an elevated PESI score might benefit from inpatient observation until clinical improvement is noted. Advanced therapies are typically not needed in these patients.

Management of acute pulmonary embolism in patients with active bleeding. In patients experiencing active bleeding or deemed as having an unacceptable risk of bleeding, both anticoagulation and especially thrombolysis are contraindicated. These individuals are typically managed with supportive therapies alone. Even if embolectomy was to be considered a final option for patients with hemodynamically significant PE following a thorough evaluation of risks and benefits, there remains a risk of significant residual and distal pulmonary obstruction. Furthermore, recurrent embolization may occur more frequently in the absence of anticoagulation.

To mitigate the risk of recurrent PE in patients with a contraindication to anticoagulation, placement of an inferior vena cava (IVC) filter can be considered. A meta-analysis comprising 2,055 patients undergoing IVC filter placement showed a 50% reduction in the incidence of PE compared to controls without a significant effect on mortality (24). Due to a 19% rate of venous wall penetration, IVC filters are not routinely used in all patients and should be left in place for as little time as possible to minimize the risk of device-related complications (25). The US Food and Drug Administration currently recommends removing IVC filters within 25–54 days from implantation.

CONCLUSIONS

In recent years, the treatment options for patients with PE have expanded, with transcatheter therapies showing promise as emergent interventions in hemodynamically significant PE and potentially expediting the recovery process in intermediate-risk PE. This has led to a shift in clinical practice toward early VA-ECMO initiation to stabilize high-risk PE patients followed by prompt catheter-directed therapies when available, moving away from systemic thrombolysis. For intermediate-risk patients, the modality and timing of intervention are still uncertain, but several

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ongoing trials will provide invaluable information in this population. Therefore, the current ESC clinical guidelines published in 2019 already do not reflect the most recent evidence and US practice patterns in the treatment of acute PE, and we anticipate a significant change in the clinical recommendations in future societal guidelines.

DISCLOSURE STATEMENT

J.G. advises and has received research grants to the institution from Boston Scientific, Inari Medical, and Endovascular Engineering. He is part of the research committee at the Pulmonary Embolism Response Team (PERT) Consortium and is the Peripheral Vascular Disease Council Chairman at the Society for Cardiovascular Angiography & Interventions (SCAI).

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